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(74) Agents: WOODWARD, David et al.; Sidley Austin Brown & Wood LLP, 1501 K Street, N.W., Washington, D.C. 20005 (US).

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(54) Title: COMPOSITIONS AND METHODS FOR TREATING NIDDM AND OTHER CONDITIONS AND DISORDERS ASSOCIATED WITH AMPK REGULATION

(57) Abstract: Compositions and methods are provided to increase glucose uptake in a cell as well as to treat a patient suffering from a condition or disorder associated with AMPK regulation. Particularly contemplated compositions include a compound that is isolated from a plant that has AICAR-like activity. In another aspect of the invention, contemplated compositions comprise a non-insulin compound that has AICAR-like activity and activates AMPK in a cell.

AMENDED CLAIMS

received by the International Bureau on 02 July 2004
claims 2-9, 11-15 are unchanged, claims 1,10, 16 & 17 are changed

We claim:

1. A method for activating 5'-monophosphate-activated protein kinase (AMPK) in a patient in need thereof, wherein the method comprises administering to said patient a composition comprising a therapeutically effective amount of a compound that activates AMPK, wherein the compound that activates AMPK has the structure of a compound purified from an extract of ground barley malt.
2. The method of claim 1, wherein the compound that activates AMPK is purified from an extract of ground barley malt.
- 10 3. The method of claim 1, wherein the compound purified from an extract of ground barley malt is obtainable through a purification process comprising:
 - (1) fractionating the extract of ground barley malt by ion exchange chromatography into protein fractions;
 - (2) collecting one or more protein fractions; and
 - 15 (3) removing protein from the protein fractions by molecular sieving chromatography to result in a purified compound that activates AMPK.
4. The method of claim 3, wherein one or more collected protein fractions comprise a thaumatin-like protein.
- 20 5. The method of claim 4, wherein a thaumatin-like protein is removed from the one or more collected protein fractions by molecular sieving chromatography.
6. The method of claim 1, wherein the patient suffers from obesity.
7. The method of claim 1, wherein the patient suffers from insulin resistance.

(21) lowers blood glucose concentrations by decreasing hepatic glucose production and/or increasing glucose disposal in skeletal muscle; and

5 (22) ameliorates one or more conditions or disorders associated with insulin resistance syndrome through improving glucose tolerance, improving lipid profile or reducing systolic blood pressure.

10 10. A method for treating a patient suffering from a condition or disorder associated with AMPK regulation, wherein the method comprises administering to said patient a composition comprising a therapeutically effective amount of a compound that activates AMPK, wherein the compound that activates AMPK has

15 the structure of a compound purified from an extract of ground barley malt.

11. The method of claim 10, wherein the compound that activates AMPK is purified from an extract of ground barley malt.

12. The method of claim 10, wherein the compound purified from an extract of ground barley malt is obtainable through a purification process comprising:

15 (1) fractionating the extract of ground barley malt by ion exchange chromatography into protein fractions;

20 (2) collecting one or more protein fractions; and

(3) removing protein from the protein fractions by molecular sieving chromatography to result in a purified compound that activates AMPK.

25 13. The method of claim 10, wherein the condition or disorder is obesity.

14. The method of claim 10, wherein the condition or disorder is insulin resistance.

15. The method of claim 10, wherein the condition or disorder is selected from the group consisting of: non-insulin dependent (type 2) diabetes mellitus, high blood pressure, elevated levels of triglycerides, hyperinsulinemia, elevated cholesterol,

glucose intolerance, low levels of high density lipoprotein (HDL), ischemia, hypoxia and glucocorticoid-induced apoptosis.

16. A process for purifying from an extract of ground barley malt a composition comprising a compound that activates AMPK, wherein the process comprises:

5 (1) fractionating the extract of ground barley malt by ion exchange chromatography into protein fractions;

(2) collecting one or more protein fractions; and

(3) removing protein from the protein fractions by molecular sieving chromatography to result in a purified compound that activates
10 AMPK.

17. A composition that comprises a compound that activates AMPK, wherein the compound comprises the same structure as the compound recited in claim 16 that activates AMPK.

STATEMENT UNDER ARTICLE 19 (1)

The "x" reference cited by the ISA does not defeat the novelty of the claims for the following reasons. With respect to claim 1 (and claims 2-9 by virtue of their dependence on claim 1), there is no teaching of a method for activating AMPK that employs a compound isolated from ground barley malt at a concentration effective to activate AMPK.

With respect to claim 10 (and claims 11-15 by virtue of their dependence on claim 10), there is no teaching of a treatment of a condition associated with AMPK regulation. Nor is there any teaching of a treatment that employs a compound isolated from ground barley malt at a concentration effective to activate AMPK.

With respect to claim 16, the Asahi reference fails to teach any isolation process for an AMPK activator from barley that includes ion exchange, collection of a protein fraction, and molecular sieving. Similarly, dependent claim 17 is not anticipated by the Asahi reference for the reasons set forth above.

Respectfully submitted,

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2 July 2004
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Attachment:
Substitute Claim Sheets

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/27012

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 35/78
 US CL : 424/725

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 U.S. : 424/725

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 West, Stn

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database DERWENT, ACC-NO: 1999-169889, ASAHI BEER MALT KK. 'Wheat or barley malt based snack foods - makes use of germinated wheat or barley malt which is roasted and starch is gelatinised.' AJP-11018707A, 26 January 1999, see Abstract.	1-17

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"B" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

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